



08/905709

CofC

Dkt. 52876/JPW/LAD/AJC

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : David Stern and Ann Marie Schmidt  
Patent No. : 7,101,838 B2  
Issued : September 5, 2006  
For : A METHOD TO PREVENT ACCELERATED ATHEROSCLEROSIS USEING  
(sRAGE) SOLUBLE RECEPTOR FOR ADVANCED GLYCATION  
ENDPRODUCTS

30 Rockefeller Plaza  
New York, New York 10112  
December 4, 2009

Attn: Certificate of Correction Branch

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**Certificate**  
DEC 09 2009  
**of Correction**

REQUEST FOR A CERTIFICATE OF CORRECTION UNDER 37 C.F.R. §1.322

Patentees hereby request that the Director of the U.S. Patent and Trademark Office issue a Certificate of Correction under 37 C.F.R. §1.322 in connection with the above-identified patent. Specifically, 37 C.F.R. §1.322 (a)(1) states that "[t]he Director may issue a certificate of correction pursuant to 35 U.S.C. 254 to correct a mistake in a patent, incurred through the fault of the Office, which mistake is clearly disclosed in the records of the Office: (i) at the request of the patentee or patentee's assignee."

Patentees attach hereto as **Exhibit A**, Form PTO/SB/44 (PTO-1050) indicating the corrections to be made in the subject patent. The corrections are as follows:

The priority of the subject application should read as follows:

This application is a continuation-in-part of U.S. Serial No.  
08/592,070, filed January 26, 1996 and U.S. Serial No.

Applicants: David Stern and Ann Marie Schmidt  
U.S. Patent No: 7,101,838 B2  
Issued: September 5, 2006  
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08/755,235, filed November 22, 1996, the contents of which are hereby incorporated by reference in their entireties.

Patentees maintain that the errors in presenting incorrect priority claim on the front page of the issued U.S. Patent 7,101,838 B21, occurred as a result of an error by the U.S. Patent and Trademark Office and this error is clearly disclosed in the records of the U.S. Patent and Trademark Office. Specifically, Patentees amended page 1 of the subject specification to include a priority paragraph in a Request For Continued Prosecution Application, Supplemental Information Disclosure Statement And Preliminary Amendment filed May 11, 2001 with the United States Patent and Trademark Office in connection with the above-identified application.

A copy of the May 11, 2001 Request is attached hereto as **Exhibit B**. A copy of the signed Declaration and Power of Attorney indicating that the subject application claims benefit under Title 35, United States Code, Section 120 to U.S. Serial No. 08/592,070, filed January 26, 1996, and U.S. Serial No. 08/755,235, filed November 22, 1996, which was filed with the May 11, 2001 Request, is attached hereto as **Exhibit C**. Patentees further amended the priority paragraph in response to a June 29, 2001 Office Action in an Amendment filed December 28, 2001 with the United States Patent and Trademark Office (received at the Office on February 6, 2002) in connection with the subject application. A copy of the December 28, 2001 Amendment is attached hereto as **Exhibit D**.

As set forth in the December 28, 2001 Amendment, the purpose for perfecting the priority under 35 U.S.C. §120 was to overcome a rejection under 35 U.S.C. §102(e) of anticipation by Morser et al., U.S. Patent No. 5,864,018.

In an Amendment in Response to March 18, 2005 Office Action and Petition for a One-Month Extension of Time, attached hereto as **Exhibit E**, Patentees responded to the Examiner's allegation that the priority application, U.S. Serial No. 08/592,070, provides no support for a "derivative" of sRAGE by amending claim 1, without prejudice, to no longer recite the term

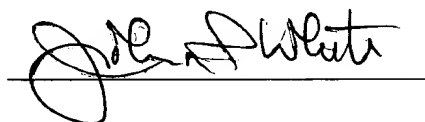
Applicants: David Stern and Ann Marie Schmidt  
U.S. Patent No: 7,101,838 B2  
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Page 3

"derivative" with respect to sRAGE. Thereafter, a Notice of Allowance was issued in connection with the subject application on September 26, 2005.

On behalf of Patentees, the undersigned respectfully requests that the Director issue a Certificate of Correction reflecting the correct priority data as set forth above in the subject Patent.

No fee is deemed necessary in connection with the filing of this Request under 37 C.F.R. §1.322. However, if any fee is necessary, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

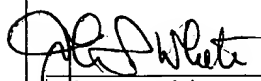
Respectfully submitted,



I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

ATTN: Certificate of Corrections Branch  
Commissioner for Patents,  
P.O. Box 1450  
Alexandria, VA 22313-1450

John P. White  
Registration No. 28,678  
Attorney for Patentees  
Cooper & Dunham LLP  
30 Rockefeller Plaza  
New York, NY 10112  
(212) 278-0400

 12/4/09  
\_\_\_\_\_  
John P. White Date  
Reg. No. 28,678

# **EXHIBIT A**

## UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO. : 7,101,838 B2  
DATED : September 5, 2006  
INVENTOR(S) : David Stern and Ann Marie Schmidt

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

The priority of the subject application should read as follows:

This application is a continuation-in-part of U.S. Serial No. 08/592,070, filed January 26, 1996, and U.S. Serial No. 08/755,235, filed November 22, 1996, the contents of which are hereby incorporated by reference in their entireties.

### MAILING ADDRESS OF SENDER:

John P. White, Esq.  
Cooper & Dunham LLP  
30 Rockefeller Plaza, 20th Flr.  
New York, NY 10112

PATENT NO. 7,101,838 B2

No. of additional copies



This collection of information is required by 37 CFR 1.322, 1.323, and 1.324. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1.0 hour to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: **Attention Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

*If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2*

Applicants : David Stern  
Ann Marie Schmidt  
U.S. Patent No. : 7,101,838  
Issued : September 5, 2006

Exhibit A

# **EXHIBIT B**



0575/52876/JPW/JML

TECH CENTER 1600/2900

MAY 16 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : David Stern and Ann Marie Schmidt # 20  
Serial No. : CPA2 of 08/905,709 Examiner: E. Lazar-Wesley  
Filing Date : March 23, 2000 Art Unit: 1646  
For : A METHOD TO PREVENT ACCELERATED  
ATHEROSCLEROSIS USING (sRAGE) SOLUBLE  
RECEPTOR FOR ADVANCED GLYCATION ENDPRODUCTS

Date of Notice  
of Allowance: February 14, 2001 Issue Batch: B87

1185 Avenue of the Americas  
New York, New York 10036  
May 11, 2001

Honorable Commissioner for Patents  
Washington, D.C. 20231

BOX: CPA

Sir:

REQUEST FOR CONTINUED PROSECUTION APPLICATION, SUPPLEMENTAL  
INFORMATION DISCLOSURE STATEMENT AND PRELIMINARY AMENDMENT

This application is a continued prosecution application ("CPA") of U.S. Serial No. 08/905,709, filed March 23, 2000. A Notice of Allowance was issued by the U.S. Patent and Trademark Office on February 14, 2001 in connection with the above-identified application and therefore an issue fee is due on May 14, 2001. This CPA application is filed herewith in lieu of paying the issue fee which is due on May 14, 2001. Applicants have enclosed the \$355.00 filing fee required for filing the CPA. Thus, this CPA, Supplemental Information Disclosure Statement and Preliminary Amendment are being timely filed.

COMMERCIAL AND CONFIDENTIAL 000000037 08905703

100.00 02

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Applicants : David Stern  
Ann Marie Schmidt  
U.S. Patent No. : 7,101,838  
Issued : September 5, 2006

Exhibit B

David M. Stern and Ann Marie Schmidt  
U.S. Serial No.: CPA2 of 08/905,709  
Filed: Herewith  
Page 2

Please amend the subject application as follows:

In the specification:

On page 1, after the title, please insert the following paragraph:

This application claims priority under 35 U.S.C. §120 of U.S. Serial No. 08/592,070, filed January 26, 1996 and U.S. Serial No. 08/755,235, filed November 22, 1996, the contents of each of which are hereby incorporated by reference in their entireties.

REMARKS

Claims 1-10, 12-27 are allowed. A Notice of Allowance was issued on February 14, 2001 and an issue fee is due May 14, 2001. Applicants are filing the present CPA and Supplemental IDS in lieu of paying the issue fee. Applicants have introduced a claim to priority to two related, co-pending U.S. applications. A new Declaration which includes reference to both U.S. Serial Nos. mentioned in the claim to priority is attached hereto as **Exhibit A**. Applicants maintain that this amendment raises no issue of new matter and requests that the Examiner enter this amendment. Thus, claims 1-10 and 12-27 are allowed.

Amendment to Priority Claim Under 35 U.S.C. §120

Applicants have amended the claim to priority under 35 U.S.C.



\*DP

David M. Stern and Ann Marie Schmidt  
U.S. Serial No.: CPA2 of 08/905,709  
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§120 hereinabove. Applicants submit herewith a new Declaration which includes reference to the two aforementioned U.S. Serial Nos. as applications to which the applicants now claim priority under 35 U.S.C. §120. Therefore, applicants request that the Examiner enter this amendment.

Supplemental Information Disclosure Statement

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following documents, which are listed hereinbelow and again listed on Form PTO-1449 attached hereto as **Exhibit B**. Copies of the documents listed below are attached hereto as **Exhibits 1-32** except that copies of Exhibits 2, 6, 7, 12, 17, 23 and 25 will be submitted shortly.

1. Brett, J, et al., (1993) "Survey of the distribution of a newly-characterized receptor for AGEs in tissues" *Am. J. Pathol*, 143:1699-1712.
2. Connolly ES, Winfree CJ, Stern DM, Solomon RA, Pinsky DJ: Procedural and strain-related variables significantly affect outcome in a murine model of focal cerebral ischemia. *Neurosurg* 1996;38:523-532.
3. Gibbons, G. H. and V. J. Dzau. (1996). Molecular therapies for vascular diseases. Science 272: 689-693.

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Filed: Herewith  
Page 4

4. Hori, et al. "The Receptor for Advanced Glycation Endproducts: Implications for the Development of Diabetic Vascular Disease. Fundam. Clin. Cardiol." In: The Endothelium in Clinical Practice. January 1997, Chapter 11, pages 311-329.
5. Khoury, J., et al., (1994) "Macrophages adhere to glucose-modified basement membrane via their scavenger receptors" *J. Biol. Chem.*, 269:10197-10200.
6. Kindy, S. Mark and Rader, J. Daniel (1998) "Reduction in Amyloid A Amyloid Formation in Apolipoprotein-E-Deficient Mice," *American Journal of Pathology* 152:1387-1395.
7. Marui, N., et al. (1993) "VCAM-1 gene transcription and expression are regulated through an oxidant-sensitive mechanism in human vascular endothelial cells" *J. Clin. Invest.*, 92:1866-1874.
8. Morser et al., U.S. Patent No. 5,864,018, filing date April 16, 1996.
9. Morser et al. PCT International Application No. PCT/EP97/01834, filed April 11, 1997, published October 23, 1997; Publication No. WO 97/39125, Antibodies Against the Advanced Glycation Endproduct Receptor and Uses Thereof.
10. Morser et al. PCT International Application No.

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Filed: Herewith  
Page 5

PCT/EP97/01832, filed 11 April 1997, published October 23, 1997, Publication No. WO 97/39121, Advanced Glycation Endproduct Receptor Peptides and Uses Thereof.

11. Nakamura, Y. et al. (1993) Immunohistochemical localization of advanced glycosylation endproducts in coronary atheroma and cardiac tissue in diabetes mellitus. *Am. J. Pathol.* 143(6):1649-1656.
12. Nakashima Y, Plump A, Raines E, Breslow J, Ross R: ApoE-deficient mice develop lesions of all phases of atherosclerosis throughout the arterial tree. *Arterioscler Thromb* 1994;141:133-140.
13. Neeper, M., et al. (1992). Cloning and expression of a cell surface receptor for advanced glycosylation end products of proteins. *J. Biol. Chem.* 267: 14998-15004.
14. Palinski, W. et al. (1995) Immunological evidence for the presence of advanced glycation end products in atherosclerotic lesions of euglycemic rabbits. *Arterioscl. Thromb. And Vasc. Biol.* 15(5):571-582.
15. Park, L., et al. (1998) "Suppression of accelerated diabetic atherosclerosis by soluble Receptor for AGE (sRAGE)" *Nature Medicine*, 4:1025-1031.
16. Park, L., et al. (1997). A murine model of accelerated

diabetic atherosclerosis: suppression by soluble receptor for advanced glycation endproducts. Circulation Supplement. Abstract 3079

17. Ritthaler, et al. (1995) Expression of receptors for advanced glycation end products in peripheral occlusive vascular disease. *Am. J. Path.* 146:688-694.
18. Schmidt, A. M. et al. (1993) Regulation of human mononuclear phagocyte migration by cell surface-binding proteins for advanced glycation end products. *J. Clin. Invest.* 92:2155-2168.
19. Schmidt, A. M., et al. (1997) "The V-Domain of Receptor for Advanced Glycation Endproducts (RAGE) mediates binding of AGEs: a novel target for therapy of diabetes" *Circulation Supplement*, 96:#194, p. I -37.
20. Schmidt, A-M, et al. (1994) "Cellular receptors for advanced glycation end products" *Arterioscler. Thromb.*, 14:1521-1528.
21. Schmidt, A. M., et al (1995) "The Dark Side of Glucose (News and Views)" *Nature Medicine*, 1:1002-1004.
22. Schmidt, A-M, et al. (1994) "Receptor for advanced glycation endproducts (AGEs) has a central role in vessel wall interactions and gene activation in response to circulating AGE proteins" *Proc. Natl. Acad. Sci. (USA)*, 91:8807-8811.

David M. Stern and Ann Marie Schmidt  
U.S. Serial No.: CPA2 of 08/905,709  
Filed: Herewith  
Page 7

23. Schmidt A-M, Yan S-D, Wautier J-L, Stern DM: Activation of RAGE: a mechanism for chronic dysfunction in diabetic vasculopathy and atherosclerosis. *Circ Res* 1999;84:489-497.
24. Stern et al., PCT International Publication No. **WO 97/26913**, published July 31, 1997, PCT International Application No. PCT/US97/00857 (Attny Dkt 48316-PCT).
25. Stern, D., AM Schmidt and Jun Wu - PCT International Publication No. **WO/98/22138** Published May 28, 1998, PCT International Application No. PCT/US97/21197 filed November 12, 1997 A Method For Treating Symptoms Of Diabetes In A Subject (Attny Dkt. 50159-PCT).
26. U.S. Patent No. 5,688,653, November 18, 1997 (Ulrich, et al.).
27. Vlassara et al., **US Patent 5,585,344**.
28. Vlassara, H., et al. (1995) "Identification of Galectin-2 as a high affinity binding protein for Advanced Glycation Endproducts (AGE): a new member of the AGE-Receptor complex" Molecular Medicine, 1:634-646.
29. Vlassara, H., et al. (1994). Pathogenic effects of advanced glycosylation: biochemical, biologic, and clinical implications for diabetes and aging. Lab. Invest. 70: 138-

David M. Stern and Ann Marie Schmidt  
U.S. Serial No.: CPA2 of 08/905,709  
Filed: Herewith  
Page 8

151.

30. Wautier, J. L., et al. (1996) "Receptor-mediated endothelial dysfunction in diabetic vasculopathy: sRAGE blocks hyperpermeability in diabetic rats" *J. Clin. Invest.*, 97 (1):238-243.
31. Wautier, J.-L., et al. (1996). Interaction of diabetic erythrocytes bearing advanced glycation endproducts with the endothelial receptor AGE induces generation of reactive oxygen intermediates and cellular dysfunction. Circulation Supplement 94(8): #4139.
32. Yan, S-D., et al. (1994) "Enhanced cellular oxidant stress by the interaction of advanced glycation endproducts with their receptors/binding proteins" *J. Biol. Chem.*, 269:9889-9897.

The fee for filing a Supplemental Information Disclosure Statement under 37 C.F.R. §1.17(p) is \$180.00 and a check including this amount is enclosed herewith. Applicants request the Examiner make these references of record.

Early and favorable action is respectfully requested.

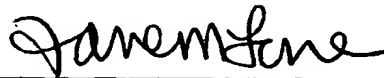
If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number

David M. Stern and Ann Marie Schmidt  
U.S. Serial No.: CPA2 of 08/905,709  
Filed: Herewith  
Page 9

provided below.

No fee other than the \$355.00 CPA filing fee and the \$180.00 IDS fee, is deemed necessary in connection with the filing of this CPA, Supplemental IDS and Preliminary Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



---

John P. White  
Registration No. 28,678  
Jane M. Love  
Registration No. 42,812  
Attorneys for Applicants  
Cooper & Dunham, LLP  
1185 Avenue of the Americas  
New York, New York 10036  
(212) 278-0400

# **EXHIBIT C**





0575/52876/JPW/JML

### DECLARATION AND POWER OF ATTORNEY

As a below-named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought, on the invention entitled:

A METHOD TO PREVENT ACCELERATED ATHEROSCLEROSIS USING (sRAGE) SOLUBLE RECEPTOR FOR ADVANCED GLYCATION ENDPRODUCT

the specification of which:  
(check one)

\_\_\_ is attached hereto.

X was filed on August 5, 1997 as

Application Serial No. 08/905,709

and was amended April 1, 1999; October 25, 1999; and  
December 15, 2000 (if applicable)

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the U.S. Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119 (a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International Application which designated at least one country other than the United States, listed below. I have also identified below any foreign application for patent or inventor's certificate, or PCT International Application having a filing date before that of the earliest application from which priority is claimed:

Prior Foreign Application(s)

Priority Claimed

<u>Number</u>	<u>Country</u>	<u>Filing Date</u>	<u>Yes</u>	<u>No</u>
N/A				

Applicants : David Stern  
Ann Marie Schmidt  
U.S. Patent No. : 7,101,838  
Issued : September 5, 2006

Exhibit C

Applicants: David Stern and Ann-Marie Schmidt

U.S. Serial No: 08/905,709

Filed: August 5, 1997

***Declaration and Power of Attorney***

Page 2

*I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below:*

<u>Provisional Application No.</u>	<u>Filing Date</u>	<u>Status</u>
N/A		

*I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States Application(s), or Section 365(c) of any PCT International Application(s) designating the United States listed below. Insofar as this application discloses and claims subject matter in addition to that disclosed in any such prior Application in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56, which became available between the filing date(s) of such prior Application(s) and the national or PCT international filing date of this application:*

<u>Application Serial No.</u>	<u>Filing Date</u>	<u>Status</u>
08/592,070	January 26, 1996	Pending
08/755,235	November 22, 1996	Pending

***And I hereby appoint***

John P. White (Reg. No. 28,678); Christopher C. Dunham (Reg. No. 22,031); Norman H. Zivin (Reg. No. 25,385); Jay H. Maioli (Reg. No. 27,213); William E. Pelton (Reg. No. 25,702); Robert D. Katz (Reg. No. 30,141); Peter J. Phillips (Reg. No. 29,691); Wendy E. Miller (Reg. No. 35,615); Richard S. Milner (Reg. No. 33,970); Robert T. Maldonado (Reg. 38,232); Paul Teng (40,837); Richard F. Jaworski (Reg. No. 33,515); Elizabeth M. Wieckowski (Reg. No. 42,226); Pedro C. Fernandez (Reg. No. 41,741); Gary J. Gershik (Reg. No. 39,992); Jane M. Love (Reg. No. 42,812); Spencer H. Schneider (Reg. No. 45,923) and Raymond A. Diperna (Reg. No. 44,063).

*and each of them, all c/o Cooper & Dunham LLP, 1185 Avenue of the Americas, New York, New York 10036, my attorneys, each with full power of substitution and revocation, to prosecute this application, to make alterations and amendments therein, to receive the patent, to transact all business in the Patent and Trademark Office connected therewith and to file any International Applications which are based thereon under the provisions of the Patent Cooperation Treaty.*

Applicants: David Stern and Ann-Marie Schmidt

U.S. Serial No.: 08/905,709

Filed: August 5, 1997

*Declaration and Power of Attorney*

Page 3

Please address all communications, and direct all telephone calls, regarding this application to:

John P. White \_\_\_\_\_ Reg. No. 28,678  
Cooper & Dunham LLP  
1185 Avenue of the Americas  
New York, New York 10036  
Tel. (212) 278-0400

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first joint inventor \_\_\_\_\_ David Stern

Inventor's signature \_\_\_\_\_ David Stern

Citizenship United States of America Date of signature 4/26/01

Residence 63 Tanners Road, Great Neck, New York 11020, USA

Post Office Address \_\_\_\_\_ Same as above

Full name of joint inventor (if any) \_\_\_\_\_ Ann-Marie Schmidt

Inventor's signature \_\_\_\_\_

Citizenship United States of America Date of signature 4/26/01

Residence 242 Haven Road, Franklin Lakes, New Jersey, 07417, USA

Post Office Address \_\_\_\_\_ Same as above

Full name of joint inventor (if any) \_\_\_\_\_

Inventor's signature \_\_\_\_\_

Citizenship \_\_\_\_\_ Date of signature \_\_\_\_\_

Residence \_\_\_\_\_

Post Office Address \_\_\_\_\_

# **EXHIBIT D**

In re Application of: David Stern and Ann-Marie Schmidt

Serial No.: 08/905,709

Examiner: E. Lazar-Wesley

Filed: August 5, 1997

Group Art Unit: 1646

For: A METHOD TO PREVENT ACCELERATED ATHEROSCLEROSIS USING  
(SRAGE) SOLUBLE RECEPTOR FOR ADVANCED GLYCATION ENDPRODUCTS

HONORABLE ASSISTANT COMMISSIONER FOR PATENTS  
Washington, D.C. 20231

December 28, 2001

S I R:

Transmitted herewith is an amendment to the above-identified application.

X  Small entity status of this application under 37 C.F.R. \$1.9 and \$1.27 has been established by a verified statement previously submitted.

A verified statement to establish small entity status under 37 C.F.R. \$1.9 and \$1.27 is enclosed.

X  No additional fee is required.

The filing fee is calculated as follows:

	NUMBER AFTER AMEND- MENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		NUMBER OF EXTRA CLAIMS PRESENTED		RATE FEE				
							SMALL ENTITY	OTHER ENTITY		SMALL ENTITY	OTHER ENTITY
Total Claims	13	-	* 30	=	0	X	\$9	\$18	=	\$ 0	0
Indepen- dent Claims	1	-	** 5	=	0	X	\$42.00	\$84.00	=	0	0
Multiple Dependent Claim(s) Presented <u> </u> Yes <u> X </u> No For First Time							\$140	\$280	0	0	0
							TOTAL ADDITIONAL FEE \$0.00				

\*If the "HIGHEST NUMBER PREVIOUSLY PAID FOR" is less than 20, write "20" in this space.

\*\*If the "HIGHEST NUMBER PREVIOUSLY PAID FOR" is less than 3, write "3" in this space.

\*\*If the difference between the "NUMBER AFTER AME" the "HIGHEST NUMBER PREVIOUSLY PAID FOR" is "0", write "0" in the space.

Applicants : David Stern  
Ann Marie Schmidt  
U.S. Patent No. : 7,101,838  
Issued : September 5, 2006

Exhibit D

Applicants: David Stern and Ann-Marie Schmidt  
Serial No.: 08/905,709  
Filed : August 5, 1997

Amendment Transmittal Letter  
Page 2

The "HIGHEST NUMBER PREVIOUSLY PAID FOR" (Total or Independent) is the highest of the "NUMBER AFTER AMENDMENT" in any prior amendment or the number of claims as originally filed.

\_\_\_\_\_ Please charge Deposit Account No. \_\_\_\_\_  
in the amount of \$ \_\_\_\_\_.

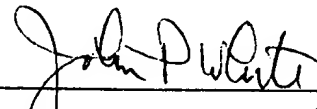
X A check in the amount of \$ 460.00 is enclosed.

X The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 03-3125. Three copies of this sheet are enclosed.

X Any filing fees under 37 C.F.R. \$1.16 for the presentation of extra claims.

X Any patent application processing fees under 37 C.F.R. \$1.17.

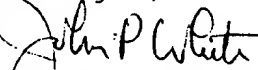
Respectfully submitted,



John P. White  
Registration No. 28,678  
Attorney for Applicants  
Cooper & Dunham LLP  
1185 Avenue of the Americas  
New York, New York 10036  
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. postal Service with sufficient postage as first class mail in an envelope addressed to:

Assistant Commissioner of Patents  
Washington, DC 20231



12/28/01

John P. White  
Reg. No. 28,678

Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: David Stern and Ann-Marie Schmidt  
Serial No.: 08/905,709                      Group Art Unit: 1646  
Filed : August 5, 1997                      Examiner: E. Lazar-Wesley  
For : A METHOD TO PREVENT ACCELERATED ATHEROSCLEROSIS  
USING (sRAGE) SOLUBLE RECEPTOR FOR ADVANCED  
GLYCATION ENDPRODUCTS

1185 Avenue of the Americas  
New York, New York 10036  
December 28, 2001

Assistant Commissioner for Patents  
Washington, DC 20231

SIR:

**AMENDMENT IN RESPONSE TO  
JUNE 29, 2001 OFFICE ACTION, CONFIRMATION OF  
SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT FILED ON  
MAY 11, 2001 AND PETITION FOR A THREE-MONTH EXTENSION OF TIME**

This Amendment is submitted in response to a June 29, 2001 Office Action issued by the United States Patent and Trademark Office in connection with the above-identified application. A response to the June 29, 2001 Office Action was originally due September 29, 2001. Applicants hereby petition for a three-month extension of time. Applicants have previously established small entity status. The required fee for a three-month extension of time for a small entity is \$460.00 and a check in this amount is enclosed. Therefore, a response to the June 29, 2001 Office Action is now due December 29, 2001. Accordingly, this Amendment is being timely

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filed.

Please amend the subject application as follows:

In the specification:

Please amend the paragraph on page 1, lines 6-9, under the provisions of 37 C.F.R. §1.121(c) as follows. A marked up version of the amended specification wherein the deleted material is in brackets and the inserted material is underlined is attached hereto as Exhibit A.

--This application is a continuation-in-part of U.S. Serial No. 08/592,070, filed January 26, 1996 and U.S. Serial No. 08/755,235, filed November 22, 1996, the contents of which are hereby incorporated by reference in their entirety.--

In the claims:

Please amend claims 1 and 16 under the provisions of 37 C.F.R. § 1.121(c) as follows. A marked up version of amended claim 1 and 16 wherein the deleted material is in brackets and the inserted material is underlined is attached hereto as Exhibit B. Please also add new claims 36-46.

- 1. (Amended) A method of preventing atherosclerosis in a subject suffering from hyperlipidemia which comprises administering to the subject a polypeptide which is an agent capable of inhibiting an interaction between AGE



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and RAGE in an amount effective to prevent atherosclerosis in the subject.--

--16. (Amended)The method of claim 1, wherein the administering is effected by intralesional, intraperitoneal, intramuscular or intravenous injection, infusion, liposome-mediated delivery, or topical, nasal, oral, ocular or otic delivery.--

--36. (New)The method of claim 1, wherein the hyperlipidemia is hypercholesterolemia.--

--37. (New)The method of claim 1, wherein the hyperlipidemia is hypertriglyceridemia.--

--38. The method of claim 1, wherein the agent is a soluble extracellular portion of a receptor for advanced glycation endproduct (RAGE).--

--39. (New)The method of claim 1, wherein the agent is soluble receptor for advanced glycation endproduct (sRAGE).--

--40. (New)The method of claim 1, wherein the agent is an antibody or portion thereof capable of specifically binding to RAGE.--

--41. (New)The method of claim 40, wherein the antibody is a

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monoclonal antibody.--

- 42. (New)The method of claim 40, wherein the antibody is a polyclonal antibody.--
- 43. (New)The method of claim 40, wherein the portion of the antibody is a complementarity determining region.--
- 44. (New)The method of claim 40, wherein the portion of the antibody is a variable region.--
- 45. (New)The method of claim 40, wherein the portion of the antibody is an Fab portion.--
- 46. (New)The method of claim 1, wherein the polypeptide is admixed with a pharmaceutically acceptable carrier.--

#### REMARKS

Claims 1-10, 12, 13, 15-27, 29, 30 and 32-35 are pending in the subject application. Applicants have hereinabove canceled claims 5-7, 10, 12, 13, 19-27, 29, 30 and 32-35 without prejudice or disclaimer to applicants' right to pursue the subject matter of these claims in a later-filed application. Further, applicants have amended claims 1 and 15-18 and added new claims 36-45. Support may be found inter alia in the specification as follows: claim 1: page 16, line 35 ad page 17, lines 1-8; claim 15: page 6, lines 6-9; claim 16: page 6, lines 9-12; claim 17: page 6, lines 14-17;

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claim 18: page 6, lines 19-25; claim 36: page 5, lines 11-13; claim 37: page 5, lines 13-14; claim 38: page 8, lines 32-34; claim 39: page 8, lines 31-32; claim 40: page 8, lines 34-35 and page 9, lines 1-2; claim 41: page 9, line 2; claim 42: page 9, lines 2-3; claim 43: page 9, line 4; claim 44: page 9, line 4; claim 45: page 9, line 3. This amendment does not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested such that claims 1, 15-18 and 36-45 will be pending.

#### Priority

The Examiner stated that the applicant's claim for priority under 35 U.S.C. 120 is acknowledged. The Examiner alleged that U.S. Serial No. 08/592,070, filed January 26, 1996, and U.S. Serial No. 08/755,235, filed November 22, 1996, upon which priority is claimed fail to provide adequate support under 35 U.S.C. 112 for the claims of this application. The Examiner alleged that U.S. Serial No. 08/592,070 and U.S. Serial No. 08/755,235 do not support claims to methods to prevent accelerated development of atherosclerosis, or to inhibit progression of a macrovessel disease, which comprise administering the V-domain of sRAGE.

In response, applicants respectfully traverse the Examiner's above rejection. Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove amended claim 1 which recites as follows: "A method of preventing atherosclerosis in a subject suffering from hyperlipidemia which comprises administering

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to the subject a polypeptide which is an agent capable of inhibiting an interaction between AGE and RAGE in an amount effective to prevent atherosclerosis in the subject." Applicants contend that U.S. Serial No. 08/592,070 (hereinafter "'070 application"), filed January 26, 1996, and U.S. Serial No. 08/755,235 (hereinafter "'235 application"), filed November 22, 1996 adequately support the pending claims.

In support, the '070 application recites in-part at page 11, lines 3-5, that the invention provides for a method of "inhibiting interaction of an amyloid- $\beta$  peptide with a receptor for advanced glycation endproduct." Further, the '070 application recites in-part at page 13, lines 25-33, that "administering to the subject an agent capable of inhibiting the interaction of the amyloid- $\beta$  peptide with the receptor for advanced glycation endproducts" treats conditions such as "diabetes" and "hyperlipidemic atherosclerosis." Since the claimed invention relates to a method of preventing atherosclerosis in a subject suffering from hyperlipidemia by administering an inhibitor of receptor for advanced glycation endproducts, the '070 application provides support for the claims. Thus, the claimed invention is entitled to an effective filing date of January 26, 1996 (i.e. the filing date of the '070 application).

In response to the Examiner's comments regarding a lack of support in the '070 and '235 application for claims inhibiting progression of a macrovessel disease, applicants without conceding the

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correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove canceled claims 19-27, 29, 30 and 32-35 without prejudice or disclaimer to applicants' right to pursue the subject matter of this claim in a later-filed application. Claims 19-27, 29, 30 and 32-35 recite methods of inhibiting progression of macrovessel disease. Applicants contend that this amendment obviates the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

#### Continuation-in-part

The Examiner alleged that applicant has not specified how the parent cases are related to the instant application, i.e. if they are a continuation-in-part. The Examiner stated that the priority date for this application remains August 05, 1997, which is the filing date of application 08/905,709.

In response, applicants have amended the paragraph on page 1, lines 6-9, such that it now provides that the subject application is a continuation-in-part of U.S. Serial No. 08/592,070, filed January 26, 1996 and U.S. Serial No. 08/755,235, filed November 22, 1996. Applicants contend that this amendment obviates the above objection and respectfully request that the Examiner reconsider and withdraw this ground of objection.

#### Confirmation of the Information Disclosure Statement

The Examiner stated that the Information Disclosure Statement (PTO

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1449) has been received. The Examiner stated that as indicated on the IDS signed by the Examiner, some references have not been considered as they have not been provided by Applicants.

In response, applicants will send at a later date the references allegedly not received by the patent office, i.e. below listed references 2, 6, 7, 12, 17, 23 and 25. As confirmation of the information disclosure statement filed on May 11, 2001, and to ensure consideration of all references listed on Form PTO-1449, applicants list below all 32 references. Please note that copies of below listed references 1, 3-5, 8-11, 13-16, 18-22, 24 and 26-32 were provided in the information disclosure statement filed on May 11, 2001. Applicants understand that all below listed references, i.e. 1-32, will be considered upon receipt of the references allegedly not received by the patent office, i.e. below listed references 2, 6, 7, 12, 17, 23 and 25.

1. Brett, J, et al., (1993) "Survey of the distribution of a newly-characterized receptor for AGEs in tissues" *Am. J. Pathol*, 143:1699-1712.
2. Connolly ES, Winfree CJ, Stern DM, Solomon RA, Pinsky DJ: Procedural and strain-related variables significantly affect outcome in a murine model of focal cerebral ischemia. *Neurosurg* 1996;38:523-532.
3. Gibbons, G. H. and V. J. Dzau. (1996). Molecular therapies for

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vascular diseases. Science 272: 689-693.

4. Hori, et al. "The Receptor for Advanced Glycation Endproducts: Implications for the Development of Diabetic Vascular Disease. Fundam. Clin. Cardiol." In: The Endothelium in Clinical Practice. January 1997, Chapter 11, pages 311-329.
5. Khoury, J., et al., (1994) "Macrophages adhere to glucose-modified basement membrane via their scavenger receptors" *J. Biol. Chem.*, 269:10197-10200.
6. Kindy, S. Mark and Rader, J. Daniel (1998) "Reduction in Amyloid A Amyloid Formation in Apolipoprotein-E-Deficient Mice," *American Journal of Pathology* 152:1387-1395.
7. Marui, N., et al. (1993) "VCAM-1 gene transcription and expression are regulated through an oxidant-sensitive mechanism in human vascular endothelial cells" *J. Clin. Invest.*, 92:1866-1874.
8. Morser et al., U.S. Patent No. 5,864,018, filing date April 16, 1996.
9. Morser et al. PCT International Application No. PCT/EP97/01834, filed April 11, 1997, published October 23, 1997; Publication No. WO 97/39125, Antibodies Against the Advanced Glycation Endproduct Receptor and Uses Thereof.

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10. Morser et al. PCT International Application No. PCT/EP97/01832, filed 11 April 1997, published October 23, 1997, Publication No. WO 97/39121, Advanced Glycation Endproduct Receptor Peptides and Uses Thereof.
11. Nakamura, Y. et al. (1993) Immunohistochemical localization of advanced glycosylation endproducts in coronary atheroma and cardiac tissue in diabetes mellitus. *Am. J. Pathol.* 143(6):1649-1656.
12. Nakashima Y, Plump A, Raines E, Breslow J, Ross R: ApoE-deficient mice develop lesions of all phases of atherosclerosis throughout the arterial tree. *Arterioscler Thromb* 1994;141:133-140.
13. Neeper, M., et al. (1992). Cloning and expression of a cell surface receptor for advanced glycosylation end products of proteins. *J. Biol. Chem.* 267: 14998-15004.
14. Palinski, W. et al. (1995) Immunological evidence for the presence of advanced glycation end products in atherosclerotic lesions of euglycemic rabbits. *Arterioscl. Thromb. And Vasc. Biol.* 15(5):571-582.
15. Park, L., et al. (1998) "Suppression of accelerated diabetic atherosclerosis by soluble Receptor for AGE (sRAGE)" *Nature Medicine*, 4:1025-1031.



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16. Park, L., et al. (1997). A murine model of accelerated diabetic atherosclerosis: suppression by soluble receptor for advanced glycation endproducts. Circulation Supplement. Abstract 3079
17. Ritthaler, et al. (1995) Expression of receptors for advanced glycation end products in peripheral occlusive vascular disease. *Am. J. Path.* 146:688-694.
18. Schmidt, A. M. et al. (1993) Regulation of human mononuclear phagocyte migration by cell surface-binding proteins for advanced glycation end products. *J. Clin. Invest.* 92:2155-2168.
19. Schmidt, A. M., et al. (1997) "The V-Domain of Receptor for Advanced Glycation Endproducts (RAGE) mediates binding of AGEs: a novel target for therapy of diabetes" *Circulation Supplement*, 96:#194, p. I -37.
20. Schmidt, A-M, et al. (1994) "Cellular receptors for advanced glycation end products" *Arterioscler. Thromb.*, 14:1521-1528.
21. Schmidt, A. M., et al (1995) "The Dark Side of Glucose (News and Views)" *Nature Medicine*, 1:1002-1004.
22. Schmidt, A-M, et al. (1994) "Receptor for advanced glycation endproducts (AGEs) has a central role in vessel wall

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interactions and gene activation in response to circulating AGE proteins" *Proc. Natl. Acad. Sci. (USA)*, 91:8807-8811.

23. Schmidt A-M, Yan S-D, Wautier J-L, Stern DM: Activation of RAGE: a mechanism for chronic dysfunction in diabetic vasculopathy and atherosclerosis. *Circ Res* 1999;84:489-497.
24. Stern et al., PCT International Publication No. WO 97/26913, published July 31, 1997, PCT International Application No. PCT/US97/00857 (Attny Dkt 48316-PCT).
25. Stern, D., AM Schmidt and Jun Wu - PCT International Publication No. WO/98/22138 Published May 28, 1998, PCT International Application No. PCT/US97/21197 filed November 12, 1997 A Method For Treating Symptoms Of Diabetes In A Subject (Attny Dkt. 50159-PCT).
26. U.S. Patent No. 5,688,653, November 18, 1997 (Ulrich, et al.).
27. Vlassara et al., US Patent 5,585,344.
28. Vlassara, H., et al. (1995) "Identification of Galectin-2 as a high affinity binding protein for Advanced Glycation Endproducts (AGE): a new member of the AGE-Receptor complex" *Molecular Medicine*, 1:634-646.
29. Vlassara, H., et al. (1994). Pathogenic effects of advanced

Applicants: David Stern and Ann-Marie Schmidt  
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glycosylation: biochemical, biologic, and clinical implications for diabetes and aging. Lab. Invest. 70: 138-151.

30. Wautier, J. L., et al. (1996) "Receptor-mediated endothelial dysfunction in diabetic vasculopathy: sRAGE blocks hyperpermeability in diabetic rats" *J. Clin. Invest.*, 97 (1):238-243.
31. Wautier, J.-L., et al. (1996). Interaction of diabetic erythrocytes bearing advanced glycation endproducts with the endothelial receptor AGE induces generation of reactive oxygen intermediates and cellular dysfunction. Circulation Supplement 94(8): #4139.
32. Yan, S-D., et al. (1994) "Enhanced cellular oxidant stress by the interaction of advanced glycation endproducts with their receptors/binding proteins" *J. Biol. Chem.*, 269:9889-9897.

Claim Rejections under 35 U.S.C § 102(e)

The Examiner rejected claims 1-10, 12, 13, 15-27, 29, 30, 32-35 under 35 U.S.C. 102(e) as being anticipated by Morser, U.S. Patent No. 5,864,018. The Examiner stated that the claims are to methods which comprise administering a polypeptide comprising the V-domain of sRAGE or a derivative thereof capable of inhibiting the interaction of AGE and RAGE. The Examiner stated that Morser teaches peptides like the peptide of SEQ ID No:8, which block the

Applicants: David Stern and Ann-Marie Schmidt  
Serial No.: 08/905,709  
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interaction of AGE and sRAGE (col.6, lines 41-52 and col.7, lines 13-20). The Examiner stated that while Morser defines these peptides by their sequence, these peptides constitute in fact fragments of sRAGE of about 10 amino acids in length, located in the V domain of sRAGE (see attached). The Examiner stated that the peptides of Morser are derivatives of the V-domain of sRAGE, as the specification, at page 8, line 30+, recites that: "The polypeptide may be a derivative of soluble receptor for advanced glycation end products (sRAGE). The Examiner stated that the polypeptide may be a soluble extracellular portion of a receptor for advanced glycation end product...". The Examiner stated that he teaches that the soluble peptides of the invention will comprise one of more of the Ig-like domains of the extracellular region of RAGE (col.5, lines 24-28), therefore the soluble extracellular domain (sRAGE), comprising one Ig V and two IgC domains, is envisioned. The Examiner stated that he teaches that these polypeptides are useful in treating or preventing disorders which result from excessive levels of AGEs (col.19, lines 1-24), in particular in diabetic microvasculopathy, occlusive vascular disorders and atherosclerosis. The Examiner stated that he teaches therapeutically effective amounts of the polypeptides, and methods of administration (col.19, line 48 continuing through col.20). The Examiner stated that claims 1-4, 8, 10, 13, 15-21, 25, 27, 30, 32-35 are anticipated. The Examiner stated that Claims 5-7, 9, 22-24, 26 are included in the rejections, as the methods apply to disorders that are associated with diabetes or macrovessel diseases. The Examiner stated that claims 12 and 29 are included

Applicants: David Stern and Ann-Marie Schmidt  
Serial No.: 08/905,709  
Filing Date: August 5, 1997  
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in the rejection, as the polypeptides of Morser encompass a 10 kilodalton domain of sRAGE. The Examiner stated that the peptides of SEQ ID No.: 18, 12, 13, and 5 are also fragments of sRAGE of about 10 amino acids in length, located in the V domain of sRAGE (see attached), able to block interaction of AGE and sRAGE. The Examiner stated that no claim is allowed.

In response, applicants respectfully traverse the Examiner's above rejection. The MPEP states that a rejection based on 35 U.S.C. 102(e) can be overcome by perfecting priority under 35 U.S.C. 120 by amending the specification of the application to contain a specific reference to a prior application. Applicants contend that the claimed invention is entitled to a priority date of January 26, 1996 as discussed supra at page 2. Therefore, since Morser, U.S. Patent No. 5,864,018 is only available as a reference as of August 16, 1996, i.e. after the effective filing date of the claimed invention (January 26, 1996), Morser is not available as a 102(e) reference. Applicants contend that the claimed priority date obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

#### Summary

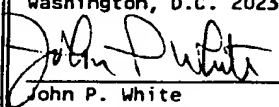
For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection and earnestly solicit allowance of the now pending claims.

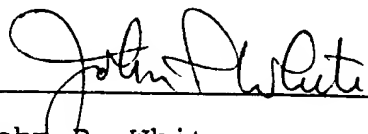
Applicants: David Stern and Ann-Marie Schmidt  
Serial No.: 08/905,709  
Filing Date: August 5, 1997  
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If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed \$460.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.	
 John P. White Reg. No. 28,678	12/28/01 Date

  
John P. White  
Registration No. 28,678  
Attorney for Applicant(s)  
Cooper & Dunham, LLP  
1185 Avenue of the Americas  
New York, New York 10036  
(212) 278-0400

# **EXHIBIT E**



Dkt. 0575/52876/JPW/AJM/JCS

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants : David M. Stern, et al.  
U.S. Serial No.: 08/905,709 Examiner: G. Chandra  
Filed : August 5, 1997 Group Art Unit: 1646  
For : A METHOD TO PREVENT ACCELERATED  
ATHEROSCLEROSIS USING (sRAGE) SOLUBLE RECEPTOR  
FOR ADVANCED GLYCATION ENDPRODUCTS

1185 Avenue of the Americas  
New York, New York 10036  
July 18, 2005

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**AMENDMENT IN RESPONSE TO MARCH 18, 2005  
OFFICE ACTION AND PETITION FOR A ONE-MONTH EXTENSION OF TIME**

This Amendment is submitted in response to a March 18, 2005 Office Action issued by the United States Patent and Trademark Office in connection with the above-identified application. A response to the March 18, 2005 Office Action was due June 18, 2005. Applicants hereby request a one-month extension of time for responding. The fee for a one-month extension of time is \$60.00 for a small entity, and a check for this amount is enclosed. With a one-month extension of time, a response is now due July 18, 2005. Accordingly, this Amendment is being timely filed.

/21/2005 HVUONG1 00000062 08905709

FC:2251

60.00 OP

Applicants : David Stern  
Ann Marie Schmidt  
U.S. Patent No.: 7,101,838  
Issued : September 5, 2006

**Exhibit E**



Applicants: David M. Stern, et al.  
U.S. Serial No.: 08/905,709  
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**Amendments to the claims**

This listing of the claims will replace all prior versions and listings of claims in the application.

1. (Currently Amended) A method of inhibiting atherosclerosis in a subject suffering from hyperlipidemia which comprises administering to the subject a polypeptide ~~comprising the amino acid sequence of~~ which comprises a soluble extracellular portion of a receptor for advanced glycation endproduct (sRAGE) ~~or a derivative thereof~~ capable of inhibiting an interaction between amyloid- $\beta$  peptide and receptor for advanced glycation endproduct (RAGE) in an amount effective to inhibit atherosclerosis in the subject.
2. (Original) The method of claim 1, wherein the subject is a mammal.
3. (Original) The method of claim 2, wherein the mammal is a human.
4. (Original) The method of claim 1, wherein the subject is a diabetic subject.
- 5-7. (Canceled)
8. (Original) The method of claim 1, wherein the subject has a glucose metabolism disorder.
9. (Original) The method of claim 1, wherein the subject is an

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obese subject.

10-14. (Canceled)

15. (Original) The method of claim 1, further comprising administering to the subject a pharmaceutically acceptable carrier during the administration of the polypeptide.

16. (Previously Presented) The method of claim 1, wherein the administering is effected by intralesional, intraperitoneal, intramuscular or intravenous injection, infusion, liposome-mediated delivery, or topical, nasal, oral, ocular or otic delivery.

17-45. (Canceled)

46. (Previously Presented) The method of claim 1, wherein the polypeptide is admixed with a pharmaceutically acceptable carrier.

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#### REMARKS

Claims 1-4, 8, 9, 15-18, 36, 37 and 46 are pending and under examination, and claims 40-45 are withdrawn, in the subject application. Claim 1 has been amended in order to more particularly point out what the applicants consider to be the invention. Support for this amendment may be found *inter alia* in the specification of priority application 08/592,070 ('070 application) at page 11, lines 28 and 29 and page 13, lines 21 to 32. Applicants maintain that the amendment of claim 1 raises no issue of new matter and is fully supported by the specification. Applicants have also canceled claims 17, 18, 36, 37 and 40-45 without prejudice. Applicants respectfully request that this Amendment be entered. Upon entry of this Amendment, claims 1-4, 8, 9, 15, 16 and 46 will be pending and under examination.

#### Claim of Priority

The Examiner asserts that the subject matter defined in claims 1-4, 8, 9, 15-18, 36, 37 and 46 has an effective filing date of August 5, 1997, which is the filing date of the subject application. The 08/592,070 application ("'070 application"), filed on January 26, 1996, allegedly fails to provide adequate support under 35 U.S.C. §112 for the instantly claimed invention.

Specifically, the Examiner alleges that the '070 application provides no support for a "derivative" of sRAGE as claimed in the instant application.

In response, and without conceding the correctness of the

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Examiner's position, applicants note that claim 1, as amended, does not recite the term "derivative" with respect to sRAGE.

Accordingly, applicants maintain that the '070 application provides adequate support under 35 U.S.C. §112 for the subject matter of pending claims 1-4, 8, 9, 15, 16 and 46, as amended. As a result, the subject matter of these claims is entitled to an effective filing date of January 26, 1996, which is the filing date of the '070 application. Applicants again note that rejected claims 17, 18, 36 and 37 have been canceled, rendering the Examiner's remarks moot with respect thereto.

**Rejection under 35 U.S.C. §112, First Paragraph**

The Examiner rejected claims 1-4, 8, 9, 15-18, 36, 37 and 46 under 35 U.S.C. §112, second paragraph, as allegedly failing to comply with the written description requirement.

Specifically, the Examiner alleges that the applicants do not provide a definition of a "derivative" or disclose any derivative in the instant application. The Examiner further alleges that derivatives of sRAGE encompass a huge number of substitutions, insertions, deletions, mutations and an attachment of modifying groups of sRAGE.

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants again point out that claim 1, as amended, does not recite the term "derivative" with respect to sRAGE. Accordingly, the Examiner's rejection of claim 1, and dependent claims 2-4, 8, 9, 15, 16 and 46, is obviated. Applicants

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again note that rejected claims 17, 18, 36 and 37 have been canceled, rendering the Examiner's rejection thereof moot.

In view of the above remarks, applicants maintain that claims 1-4, 8, 9, 15, 16 and 46 satisfy the requirements of 35 U.S.C. §112, first paragraph.

#### **Rejection Under 35 U.S.C. §102(e)**

The Examiner rejected claims 1-4, 8, 9, 15-18, 36, 37 and 46 under 35 U.S.C. 102(e) as allegedly anticipated by U.S. Patent No. 5,864,018 ("Morser"). Applicants understand this rejection to apply only to claims 1-4, 8, 9, 15, 16 and 46, as the remaining rejected claims have been canceled.

Applicants contend that the claimed invention is entitled to a priority date of January 26, 1996 as discussed above. Therefore, since Morser is only available as a reference as of April 16, 1996, i.e. after the January 26, 1996 effective filing date of the claimed invention, Morser is not available as a §102(e) reference.

In view of the above remarks, applicants maintain that claims 1-4, 8, 9, 15, 16 and 46 satisfy the requirements of 35 U.S.C. §102(e).

#### **Summary**

For the reasons set forth hereinabove, applicants respectfully request that all pending claims of this application be allowed, and that the application proceed to issuance.

Applicants: David M. Stern, et al.  
U.S. Serial No.: 08/905,709  
Filed: August 5, 1997  
Page 7

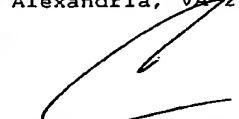
If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the \$60.00 extension fee, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:  
Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450.

  
Alan J. Morrison  
Reg. No. 37,399

Date

John P. White  
Registration No. 28,678  
Alan J. Morrison  
Registration No. 37,399  
Attorneys for Applicants  
Cooper & Dunham LLP  
1185 Avenue of the Americas  
New York, New York 10036  
Tel. No. (212) 278-0400

09646



Docket No. 0575/52876/JPW/AJM/JCS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): David M. Stern, et al.

Serial No. : 08/905,709 Examiner: G. Chandra

Filed : August 5, 1997 Group Art Unit: 1646

For : A Method To Prevent Accelerated Atherosclerosis Using (sRAGE)  
Soluble Receptor For Advanced Glycation Endproducts

Mail Stop Amendment  
 COMMISSIONER FOR PATENTS  
 P.O. Box 1450  
 Alexandria, VA 22313-1450

Date: July 18, 2005

Sir:

Transmitted herewith is an amendment to the above-identified application.

- X   Small entity status of this application under 37 C.F.R. \$1.9 and \$1.27 has been previously established.
- A verified statement to establish small entity status under 37 C.F.R. \$1.9 and \$1.27 is enclosed.
- No additional fee is required.

The filing fee is calculated as follows:

	Number after Amend-ment	Highest Number Previously Paid For <sup>1</sup>	Number of Extra Claims Presented	RATE			FEE	
				Small Entity	Other Entity		Small Entity	Other Entity
Total Claims	9 -	* 35 =	*** 0 X	\$25	\$50	=	0	
Indepen- dent Claims	1 -	** 3 =	*** 0 X	\$100	\$200	=	0	
Multiple Dependent Claim(s) Presented For First Time Yes <u>  X  </u> No				\$180	\$360	=	0	
				TOTAL ADDITIONAL FEE			\$ 0.00	

- <sup>1</sup> The "HIGHEST NUMBER PREVIOUSLY PAID FOR" (Total or Independent) is the highest of the "NUMBER AFTER AMENDMENT" in any prior amendment or the number of claims originally filed.
- \* If the "HIGHEST NUMBER PREVIOUSLY PAID FOR" is less than 20, write "20" in this space.
- \*\* If the "HIGHEST NUMBER PREVIOUSLY PAID FOR" is less than 3, write "3" in this space.
- \*\*\* If the difference between the "NUMBER AFTER AMENDMENT" and the "HIGHEST NUMBER PREVIOUSLY PAID FOR" is less than "0", write "0".

Applicant(s): David M. Stern, et al.

Serial No. : 08/905,709

Filed : August 5, 1997

Amendment Transmittal Letter

Page 2

The following are also enclosed:

☒ One additional copy of this Amendment Transmittal Letter

☒ Return Receipt Postcard

☐ An Information Disclosure Statement, including Form PTO-1449

(Copies of citations included: Yes ☐ No ☐

and a fee of \$ ☐ included)

☒ A Petition for an Extension of Time, including a fee of  
\$ 60.00 for a Petition for 1 Month(s) Extension of Time

☐ Other (identify): \_\_\_\_\_

THE TOTAL FEE DUE IS \$ 60.00.

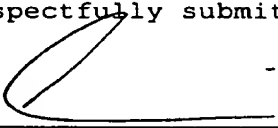
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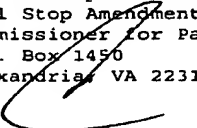
☒ The Commissioner is hereby authorized to charge any additional fees  
required or credit any overpayment to Deposit Account No. 03-3125  
as follows:

☒ Fees under 37 C.F.R. \$1.16 for the presentation of extra claims  
☐ Patent application processing fees under 37 C.F.R. \$1.17

Respectfully submitted,

  
\_\_\_\_\_  
John P. White  
Registration No. 28,678  
Alan J. Morrison  
Registration No. 37,399  
Attorneys for Applicant(s)  
Cooper & Dunham LLP (Customer #23432)  
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\_\_\_\_\_  
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Reg. No. 37,399

Date 7/18/05





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☐ Other (identify): \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

THE TOTAL FEE DUE IS \$ 60.00.

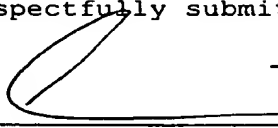
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